Methods: Allogeneic hematopoietic cell transplant (HCT) patients randomized to SIR/TAC received one year of SIR following HCT, while MTX/TAC patients received MTX on days 1, 3, 6, and 11. QOL was assessed with the Functional Assessment of Cancer Therapy – Bone Marrow Transplant Treatment Outcome Index (TOI) prior to HCT and day 30, 90, 180, 270, and 360 following HCT. Random effects models were used to examine longitudinal trajectories of QOL between day 30 and 360 by study arm, controlling for baseline TOI scores.

Results: A total of 74 patients were enrolled (37 per study arm); all contributed data to these analyses. Analyses indicated that the MTX/TAC group showed greater improvement in TOI scores over time compared to the SIR/TAC group ($P = .02$); by day 360, the average difference between groups was 7.18 points ($P = .03$). This effect continued to be significant ($P < .01$) when controlling for clinical differences between groups, including acute GVHD, chronic GVHD, and anemia. Exploratory analyses of subscales comprising the TOI [i.e., Physical Well-Being (PWB), Functional Well-Being (FWB), BMT Scale (BMTS)] indicated that group differences were due to greater improvement in PWB in the MTX/TAC group ($P = .02$). Additional exploratory analyses of items on the PWB scale indicated that members of the SIR/TAC arm were more likely to endorse a lack of energy and nausea over time (ps≤.01). Study arm differences on these items persisted when controlling for acute GVHD, chronic GVHD, and anemia (ps<.01).

Conclusions: Data from the current study indicate that SIR/TAC is associated with less improvement in QOL in the first year post-HCT compared to MTX/TAC. This difference is not attributable to other potential clinical differences between study arms, including acute and chronic GHVD and anemia. Differences in QOL appear to result in part from greater fatigue and nausea in participants treated with SIR, which was administered throughout the one year follow-up period.

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A Population-Based Cohort Study of Malignancies and Late Mortality in Children Treated by Allogeneic Stem Cell Transplantation for Non-Malignant Conditions

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Background: Characterisation of late effects in children undergoing hematopoietic stem cell transplant (HSCT) for non-malignant diseases is challenging due to the small numbers of rare diseases, variations in cancer susceptibility and organ toxicity associated with primary diagnosis as well as non-uniform clinical practice. In addition, limited follow-up in previous studies may have underestimated the risk of second cancers and late deaths in this group of transplant recipients. Our study used population-based registry data to determine the risk of malignancy and late mortality in pediatric patients transplanted for non-malignant conditions.

Methods: 318 Australian allogeneic transplant recipients aged less than 15 years, treated from 1982-2007 for non-malignant conditions, were identified from children's hospitals and the Australasian Bone Marrow Transplant Recipient Registry (ABMTRR). Clinical and demographic data were obtained from the ABMTRR and medical records. Linkage with the Australian Cancer Database and National Death Index was performed to identify all primary invasive cancers and deaths in this cohort. Standardised incidence ratios (SIRs) were generated for second malignancies and deaths in 2-year survivors.

Results: Indications for HSCT included; primary immunodeficiencies (n=130), aplastic anemia (SAA, n=71), inherited marrow failure syndromes (n=51), thalassemia (n=14) and hemophagocytic lymphohistiocytosis (n=14). Over two thirds of recipients were male (69%), while the median age at transplant was 3 years (range 0-14y) A total of 43 patients received radiation therapy as part of their conditioning regimen.

Six malignancies were identified in male patients with various diseases including Fanconi Anemia (2), Severe Aplastic Anemia (1), severe combined immune deficiency (1), Thalassemia (1) and chronic granulomatous disease (n=1). The most common second cancer was squamous cell carcinoma of the tongue. Overall there was a 15-fold increased risk of malignancy compared to the Australian general population (SIR=15.37, 95%CI=6.91-34.21).

Two thirds of patients (62%) survived for more than 2 years after HSCT, while the cumulative incidence of late death was 2.1% at 5 years from HSCT and 6.3% at 10 years from HSCT. Overall, the rate of death was 17 times greater than expected compared to the general population, with cancer being the most common cause of death.

Conclusion: These findings show an increased rate of malignancy and late death in Australian pediatric patients transplanted for non-malignant conditions compared to the general population. This confirms the need for long term surveillance to maximize the early detection of subsequent malignancies, which may occur a decade or more after HSCT.

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A Population-Based Cohort Study of Second Malignancies and Late Mortality in Children Treated by Allogeneic Stem Cell Transplantation for Hematological Malignancies

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Background: Increasing indications for transplant and improvements in early transplant outcomes have lead to an